PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference P913PC00	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/DK2004/000630	International filing date *(day/month/year)* 17 September 2004 (17.09.2004)	Priority date *(day/month/year)* 18 September 2003 (18.09.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NUEVOLUTION A/S		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 21 March 2006 (21.03.2006)
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Form PCT/IB/373 (January 2004)

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

24/3.

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REC'D 10 FEB 2005
WIPO PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK2004/000630	17.09.2004	18.09.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68, C12N15/10, C12P1/00, C07B61/00

Applicant
NUEVOLUTION A/S

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-62
	No:	Claims	63-68
Inventive step (IS)	Yes:	Claims	1-62
	No:	Claims	63-68
Industrial applicability (IA)	Yes:	Claims	1-68
	No:	Claims	

2. Citations and explanations

see separate sheet

V. Reasoned statement (Continuation)

2.1 CITATIONS

Reference is made to the following documents:

D1: WO 02/103008 A (NUEVOLUTION A/S; PEDERSEN, HENRIK; GOUILAEV, ALEX, HAAHR; SAMS, KLARNE) 27 December 2002 (2002-12-27)

D2: WO 03/025567 A (BERNARD, ANDRE; DUEBEL, STEFAN) 27 March 2003 (2003-03-27)

D3: WO 00/32823 A (PHYLOS, INC) 8 June 2000 (2000-06-08)

D4: WO 02/083951 A (NORTHEASTERN UNIVERSITY; GIESE, ROGER, W) 24 October 2002 (2002-10-24)

2.2 NOVELTY (Art. 33(2) PCT)

2.2.1 The present application does not satisfy the criterion set forth in **Article 33(2) PCT** because the subject-matter of **claims 63 - 68** is not new in respect of prior art as defined in the regulations (**Rule 64(1)-(3) PCT**), c.f. **D2** (figures 1, 2), **D3** (figures 1 - 20) and **D4** (figures 2, 3).

2.3 INVENTIVE STEP (Art. 33(3) PCT)

2.3.1 Document **D1** is considered to represent the most relevant state of the art with respect to **claim 1** and discloses a method for identifying display molecules having affinity towards molecular targets comprising the steps of mixing one or more molecular targets and a library of bifunctional compexes, each bifunctional complex of the library comprising a display molecule attached to an identifier oligonucleotide, the latter coding for said display molecule and thereby serving the template function. The codons of said identifier molecules are identified by contacting said identifiers with a pool of nucleic acid fragments under conditions allowing for hybridization, said fragments being addressably connected to an array, c.f. pages 113 - 119 and 131 - 153, figures 1, 3, 5 - 7, 8, 38 - 41 and 43 - 45 as

well as the explanatory text to these figures on pages 26, 27 and 52 and page 13, lines 16 - 26.

2.3.2 The subject-matter of **claim 1** differs in that unlike in the closest prior art, not only the display molecules, but also the molecular targets are attached to an oligonucleotide, the so called target oligonucleotide. Said oligonucleotide is able of identifying the molecular target.

2.3.3 The effect of attaching yet another oligonucleotide to the interaction partner, the molecular target, is that both oligonucleotides, the target oligonucleotide as well as the identifier oligonucleotide, can be connected with each other. In doing so, the interacting partners can be identified via their encoding sequences (target oligonucleotide and identifier oligonucleotide). This can be done via a PCR amplification reaction for which the connected oligonculeotides serve as template, c.f. pages 64, third paragraph and figures 1 - 13.

2.3.4 The problem to be solved by the subject matter of **claim 1** may therefore be regarded as providing a *simultaneous decoding technique* for *both* interacting partners (molecular target and display molecule).

2.3.5 The solution would be the attachment of a second oligonucleotide to the second interaction partner, in the present case the molecular target, and the identification of both oligonucleotides (target and identifier) connected to each other.

2.3.6 This solution can be considered as involving an inventive step (**Article 33(3) PCT**) for the following reasons:

2.3.6.1 There is no prior art suggesting the step of also attaching an encoding second oligonucleotide to the molecular target. By bringing together 2 bifunctional complexes, both equipped with encoding nucleic acid tags, the underlying invention allows for the simultaneous identification of both interaction partners by solely identifying the nucleic acid code. The invention makes possible also the application of many molecular targets to many display molecules whereby the simultaneous identification of more than one interaction can be monitored (multiplex function).

2.3.6.2 From the prior art available, the skilled in the art would not come up with the solution of the method of claim 1. The solution offered with the embodiments of

claim 1 is therefore not obvious.

2.3.7 The present application therefore satisfies the criterion set forth in **Article 33(3) PCT** and the subject-matter of **claims 1 - 62** involves an inventive step (**Rule 65(1)(2) PCT**).